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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/538,338	03/29/00	BENNER S	13238.9USC1

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EXAMINER	
ARTHUR, L	
ART UNIT	**PAPER NUMBER**
1655	6

DATE MAILED: 07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/538,338	Benner
Examiner	**Art Unit**
Lisa Athur	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *March 29, 2000 and July 18, 2000*

2a) [ ] This action is **FINAL.** 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *4-14* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *4-14* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirem

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 4,5,10,11 are rejected under 35 U.S.C. 102(b) as being anticipated by Eritja et al. (Nucleic Acids Research (1986) 14(20): 8135-8153).

Claims 4,5,10,11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eritja et al..

Eritja et al. Teach a method for making an oligonucleotide using a template containing a non-standard nucleotide, i.e. a xanthine by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the xanthine by enzymatic polymerization. (Page 8151, lines 11-33). Eritja et al. teaches that the mixture of nucleoside triphosphates included dTTP, dATP, dCTP, dUTP or dAPTP (which is 9-(beta-D-2'-deoxyribofuranosyl)-2-aminopurine triphosphate). This dAPTP is an example of a derivatized nucleotide. I t is noted that Eritja et al does not identify the xanthine as a puADA, but this characterization of xanthine does not differentiate it from the xanthine used by Eritja et al. Therefore, Eritja et al teach every limitation recited in the claims.

3. Claims 4,6,8-9,11-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Switzer et al. (J. AM CHEM SOC. (1989) 111: 8322-8323).

Switzer et al. teaches a method for making an oligonucleotide using a template containing the non-standard bases iso-G or isoC by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the isoG or isoC by enzymatic polymerization. Switzer et al. Teach labeling the nucleotide triphosphates and teaches using Klenow fragment and T7 RNA polymerase as the polymerization agent.

4. Claims 5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Switzer et al..

Switzer et al. teaches a method for making an oligonucleotide using a template containing the non-standard bases iso-G or isoC by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the isoG or isoC by enzymatic polymerization. Switzer et al. Teach labeling the nucleotide triphosphates and teaches using Klenow fragment and T7 RNA polymerase as the polymerization agent. Switzer et al. did not describe iso-G and iso-C as puDDA or puAAD, respectively, but this characterization of these compounds does not differentiate them from the iso-G and isoC of Switzer et al. These claims, however, do not have priority to parent applications 07/594,290 or 08/542,142 because these application did not include the description in the claims of isoG and isoC as puDDA and pyAAD. Therefore these claims can only claim priority back to parent application 08/775,401, filed December 31, 1996.

5. Claims 4,6,8-9,11-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Piccirilli et al.(Nature (Jan 4, 1990) 343:33-37). Piccirilli et al. teaches a method for making an oligonucleotide using a template containing the non-standard bases iso-G or isoC by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the isoG or isoC by enzymatic polymerization. Piccirilli et al. Teach labeling the nucleotide triphosphates and teaches using Klenow fragment and T7 RNA polymerase as the polymerization agent. Piccirilli et al. Teach additional non-standard base pairs predicted to function in the method of making an oligonucleotide.

6. Claims 5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Piccirilli et al..

Piccirilli et al. teaches a method for making an oligonucleotide using a template containing the non-standard bases iso-G or isoC by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the isoG or isoC by enzymatic polymerization. Piccirilli et al. Teach labeling the nucleotide triphosphates and teaches using Klenow fragment and T7 RNA polymerase as the polymerization agent. Piccirilli et al. did not describe iso-G and iso-C as puDDA or puAAD, respectively, but this characterization of these compounds does not differentiate them from the iso-G and isoC of Piccirilli et al. These claims, however, do not have priority to parent

applications 07/594,290 or 08/542,142 because these application did not include the description in the claims of isoG and isoC as puDDA and pyAAD. Therefore these claims can only claim priority back to parent application 08/775,401, filed December 31, 1996.

7. Claims 5 and 10 are rejected under 35 U.S.C. 102 (b) as being anticipated by Piccirilli et al. (Biochemistry (1991) 30: 10350-10356) or by Tor et al. (J. AM. CHEM SOC. (1993) 115: 4461-4467) or by Switzer et al. (BIOCHEMISTRY (1993) 32: 10489-10496).

Piccirilli et al. Teach a method for making an oligonucleotide using a DNA template containing a nonstandard base , i.e. methylpseudouridine, by contacting this template with an oligonucleotide in the presence of derivatized nucleotides, such that ATP or formycin triphosphate were incorporated opposite the non-standard base T7 RNA polymerase.

Tor et al. Teach method for making an oligonucleotide using an DNA template containing a nonstandard base , i.e. deoxy-5-methylisocytosine,, by contacting this template with an oligonucleotide in the presence of derivatized nucleotides, such that 6-aminohexyl-isoguanosine is incorporated opposite the non-standard base by T7 RNA polymerase.

Switzer et al. Teach method for making an oligonucleotide using an DNA template containing a nonstandard base , i.e.isocytosine or isoguanosine by contacting this template with an oligonucleotide in the presence of derivatized nucleotides, such that isoguanosine or isocytosine is incorporated opposite the non-standard base by T7 RNA polymerase.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 7,8,9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eritja et al..

Eritja et al. Teach a method for making an oligonucleotide using a template containing a non-standard nucleotide, i.e. a xanthine by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the xanthine by enzymatic polymerization. (Page 8151, lines 11-33). Eritja et al. teaches that the mixture of nucleoside triphosphates included dTTP, dATP, dCTP, dUTP or dAPTP (which is 9-(beta-D-2'-deoxyribofuranosyl)-2-aminopurine triphosphate). This dAPTP is an example of a derivatized nucleotide.

Eritja et al. Does not teach using a labeled nucleoside triphosphate during the extension reaction. However, Eritja et al does teach labeling the 5' end of the primer with a radiolabeled nucleotide, i.e 32P-ATP. Furthermore, the use of biotin, thiol and hydrazine labeled nucleotides during primer extension reactions and their incorporation by polymerases is was well known in the art. Therefore, it would have been prima facie obvious to one of ordinary skill to have modified the method of Eritja et al. By adding a label, such as a radiolabel, biotin, thiol or hydrazine, to the nucleotides to be incorporated in the primer opposite the non-standard base, xanthine, in order to

have more easily and quickly labeled the extended primer than by end labeling the primer prior ro extension which adds an additional step. Furthermore, the ordinary artisan would have been motivated to have labeled the base which incorporated opposite the non-standard base in order to easily detect that the derivatized base was able to incorporate opposite the non-standard base.

10. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Switzer et al..

Switzer et al. teaches a method for making an oligonucleotide using a template containing the non-standard bases iso-G or isoC by contacting this template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to the portion of the template containing the isoG or isoC by enzymatic polymerization. Switzer et al. Teach labeling the nucleotide triphosphates and teaches using Klenow fragment and T7 RNA polymerase as the polymerization agent. Switzer et al. Does not teach the labeling of the nucleotides to be incorporated with biotin, thiol or hydrazine. However, the use of biotin, thiol and hydrazine labeled nucleotides during primer extension reactions and their incorporation by polymerases is was well known in the art. Therefore, it would have been prima facie obvious to one of ordinary skill to have modified the method of Switzer et al. by adding a different label,, biotin, thiol or hydrazine, to the nucleotides to be incorporated in the primer opposite the non-standard base, xanthine, in order to have more easily and quickly labeled the extended primer than by end labeling the primer prior ro extension which adds an additional step. Furthermore, the ordinary artisan would have been motivated to have labeled the base which incorporated opposite the non-

standard base in order to easily detect that the derivatized base was able to incorporate opposite the non-standard base.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 4-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,432,272. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of this application and of the patent contain overlapping subject matter. The claims of this application broadly encompass the claims of patent 5,432,272 which are limited to a method of making an oligonucleotide using the specifically recited non-standard nucleotides.

13. Claims 4-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,001,983. Although the conflicting claims are not identical, they are not patentably distinct from each other because

the claims of this application are broadly drawn to methods of making oligonucleotides which include the oligonucleotide of the patent, specifically the oligonucleotides which contain iso-guanosine and iso-cytosine

14. Claims 4-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,037,120. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of this application and the claims of the patent contain overlapping subject matter. The claims of this application are drawn to methods of making oligonucleotide by binding an oligonucleotide to a template containing a non-standard base prior to primer extension. The claims of the patent are drawn to a method of binding an oligonucleotide to a template containing a non-standard base. Therefore, the claims of the patent are comprised in the method of the claims. The expression of an oligonucleotide that has been to a template is an obvious application of a method for biding an oligonucleotide to a template.

15. No claims are allowable over the prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Monday-Wednesday from 7:00 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800-1600

July 2, 2001